Please add the following new claim:

29. (New) The method of claim 17, wherein said antibody is a natural antibody, a recombinant antibody or a chimeric protein.

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

I. Status of the Claims

Claims 27 and 28 have been cancelled, without prejudice or disclaimer thereof; claims 13, 17, 18, 19, 21, 23, 24, 25, and 26 have been amended; and claim 29 has been added. Applicants reserve the right to prosecute the subject matter of the cancelled claims in this or another application.

Applicants also have incorporated into the specification, the explicit amino acid and nucleotide sequences that correspond to the database entry, Y08612, cited at page 4, line 4 of the originally-filed patent application. Explicit recitation of biological information deposited in a publicly-accessible database at the time the application was filed does not introduce new matter, since that information was inherent in applicants' disclosure of the accession number needed to access those details. Section 2406.01 of the MPEP, for example, states that biological material "must be specifically identified in the application for patent as filed." The description of "Y08612" in the present application satisfies this requirement.

Accordingly, because the amendments to the claims and specification do not introduce new matter, as discussed more fully below, entry thereof by the Examiner is respectfully requested.

II. Summary of the Invention

The claimed invention is directed to a method for diagnosing the existence of carcinomas, sarcomas, or a combination thereof, in a mammal by determining the level of expression of the protein bearing Accession number Y08612, referred to as "Nup88," in a

tissue biopsy sample. The amino acid of the protein of the Y08612 deposit has been added to the specification, as has the nucleotide sequence that encodes that protein.

The level of expression of that protein, *i.e.*, of Nup88, can be assessed by determining the quantity of an antibody that binds to the Nup88 protein. Detecting an increased level of Nup88 in a test sample compared to that in a normal sample indicates that the test sample comprises cancerous cells. In an alternative, but analogous method, the level of expression of Nup88 can be assessed by determining the level of annealing of a nucleic acid, such as a DNA or RNA probe, to a nucleic acid encoding Nup88.

III. The Office Action

A. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

1. Rejection of Claims 13-28 Under Section 112, First Paragraph, for Alleged Lack of Enablement

Claims 13-28 were rejected under 35 U.S.C. § 112, first paragraph, as it is allegedly "not clear that Nup88 is overexpressed in cancers other than breast carcinoma compared to normal control of the same tissue or cell type since no other normal controls appear to be disclosed." Office Action at page 2. Applicants respectfully disagree and traverse the rejection.

Nup88 is abundant in all cell types because it is intimately involved in the function of the cell, such as in nuclear-cytoplasmic transport. A tenet of the claimed invention is that Nup88 is overexpressed in cancer cells. For instance, Applicants show that there was no immunohistochemical staining of mucosal cells surrounding gastric cancer cells, but surprisingly the gastric cancer cells were strongly stained for Nup88. *See* page 11, line 17, of the specification. Similarly, Applicants show that cells surrounding colonic cancer cells were "negative" in stain, while the colonic cancer cells themselves were strongly reactive. *See* at page 13, line 5. Furthermore, Applicants show that ovarian cancer cells and prostate cancer cells stained positive for the overexpressed Nup88, but the remaining cells of the tissue did not. Therefore, "negative mucosa cells" described in the specification do, in fact, represent "healthy control" samples. Accordingly, it is clearly evident from Applicants' disclosure that cancer cells overexpress Nup88.

Indeed, Applicants conclude that "our findings suggest that this molecule [*i.e.*,

"Nup88"] may be a potentially significant marker *given its dramatic overexpression in a broad spectrum of malignant tumors* of literally all denominations." *See* page 20, lines 27-29. As Applicants pointed out in their previous response of April 18, 2002, the skilled artisan knows that "overexpression" is a relative term that refers to levels of expression of a particular protein beyond that normally associated with normal levels of expression of that protein.

For at least these reasons withdrawal of this ground for rejection is respectfully requested.

2. Rejection of Claims 13-28 under 35 U.S.C. § 112, First Paragraph, for Allegedly Introducing New Matter

~~Claims 13-28 were rejected under 35 U.S.C. § 112, first paragraph, as the present~~ invention allegedly "revealed that the increased expression [1.5- to 5-fold increase in expression of Nup88] is drawn only to breast cancer cells compared to normal control since no other normal controls of the same tissue are indicated . . . the specification does not reveal that this particular range was contemplated for all cancer types at the time the invention was made." Office Action at page 3. Applicants respectfully traverse the rejection.

Applicants have deleted the recitation of specific-fold increase in Nup88 protein levels as compared to control samples so as to distinguish cancer cells from non-cancer cells. Even so, the specification states at page 16, lines 17-18, that "densiometric quantification of **the blots** showed an increased expression in carcinomas between 1.5 and 5 times as compared with normal controls." That sentence does not state the densiometric quantification of the blots specifically for breast carcinomas.

Claim 13 as amended recites "a level of expression [of Nup88 in the sample] that is greater than non-cancer cells indicates that said sample comprises a cancer cell." Applicants show in Table I at page 21 of the specification numerous types of carcinomas where they recorded overexpression of Nup88, as evidenced by the "Extent of Reaction" column. The latter is an established method of identifying cells which stain positive for Nup88. Moreover, applicants teach at page 11, lines 22-24, that "the extent of the reaction [for staining intensity of cancer and non-cancerous cells] was defined by the percentage of reactive cells, and graded from negative (0) to 1+ to 5+ as previously described (Moll *et al.*, 1987, Am J Pathol 127:288-304)." Table I uses that same nomenclature to record the intensity of cell staining

and reactivity in samples comprising cancerous cell types.

Accordingly, the skilled artisan would know, from reading the specification and reviewing Table I, that determining that the expression level of Nup88 in a sample is greater than the level present in non-cancer cells indicates that the sample comprises a cancer cell.

Moreover, as Applicants point out above, adequate control samples were included in all experiments. For example, in this particular instance, lymphocytes were used as control samples; the absence of "positive" staining of Nup88 of the intensity recorded for the cancerous cell types is indicative that the lymphocytes did indeed represent a reliable control.

Thus, the "1.5 to 5" fold limitation has been removed and the amended claim is supported by the originally-filed specification. Accordingly, applicants kindly request that the examiner withdraw this rejection.

3. Rejection of Claim 22 Under Section 112, First Paragraph, for Alleged Lack of Written Description

Claim 22 was rejected under 35 U.S.C. § 112, first paragraph, as the limitation of a chimeric protein which comprises at least one CDR region of the monoclonal antibody allegedly "has no clear support" because "the specification reveals support for chimeric proteins wherein at least one CDR region of [the] monoclonal antibody is virtually identical with the corresponding counterpart of 149/1/1." Continuing, the Examiner states that in claim 22, "the absence of the limitation drawn to 'virtually identical'" causes the newly added limitation to be unsupported by the specification. Office Action at page 4. Applicants respectfully traverse the rejection.

Applicants refer to the examiner's Office Action of December 18, 2001 (Paper no. 5, page 10), where originally-filed claim 8 was rejected as being allegedly indefinite because the term 'virtually identical' "is a relative term, which is not defined in the specification . . . amending the claim to delete the term 'virtually' in line 2 can obviate this rejection."

Newly added claim 22 is equivalent to claim 8 and Applicants deliberately crafted claim 22 to avoid recitation of the term 'virtually,' as suggested by the examiner. The newly-rephrased claim 22 recites "wherein said chimeric protein comprises at least one CDR region of the monoclonal antibody bearing accession number DSM ACC 2457," **which is the same as** "[wherein] at least one CDR region of said monoclonal antibody is virtually identical with

the corresponding counterpart of 149/1/1 (DSM ACC 2457)."

Accordingly, the examiner's rejection is unfounded and Applicants respectfully request that it be withdrawn.

4. Rejection of Claim 23 Under Section 112, First Paragraph, for Alleged Lack of Written Description

Claim 23 was rejected under 35 U.S.C. § 112, first paragraph, as the examiner alleges that "the limitation of a diagnostic kit for carrying out the method of claim 13 for determining the amount of protein binding molecule in a tissue biopsy sample has no clear support in the specification and the claims as originally filed." Office Action at page 4. Applicants respectfully traverse the rejection.

Claim 23, as amended, recites a kit comprising a protein binding molecule that binds to the amino acid sequence depicted in GenBank accession number Y08612, *i.e.*, the protein sequence:

MAAAEGPVGDGELWQTWLPNHVVFLRLREGLKNQSPTEAEKPASSSLPSSPPPQLLTRNVVFGLGGELFLWDGED
SSFLVVRLRGPSGGGEEPALSQYQRLLCINPPLFEIYQVLLSPTQHHVALIGIKGLMVLELPKRWGKNSEFEGGK
STVNCSTTPVAERFFTSSTSLTLKHAAWYPSEILDPHVVLLTSDNVIRIYSLREPQTPTNVIILSEAEEESLVLN
KGRAYTASLGETAVAFDFGPLDAVPKTLFGQNGKDEVVAYPLYILYENGETFLTYISLLHSPGNIWKAVGSIAHA
SAAEDNYGYDACAVLCLPCVPNILVIATESGMLYHCVVLEGEEEDDHTSEKSWDSRIDLIPSLYVFECVELELAL
KLASGEDDPFDSDFSCPVKLHRDPKCPSRYHCTHEAGVHSVGLTWIHKLHKFLGSDEEDKDSLQELSTEQKCFVE
HILCTRPLPCRQPAPIRGFWIVPDILGPTMICITSTYECLIWPLLSTVHPASPPLLCTREDVEVAESSLRVLAET
PDSFEKHIRSILQRSVANPAFLKASEKDIAPPPEECLQLLSRATQVFREQYILKQDLAKEEIQRRVKLLCDQKKK
QLEDLSYCREERKSLREMAERLADKYEEAKEKQEDIMNRMKKLLHSFHSELPVLSDSERDMKKELQLIPDQLRHL
GNAIKQVTMKKDYQQQKMEKVLSLPKPTIILSAYQRKCIQSILKEEGEHIREMVKQINDIRNHVNF.

As the claim as amended has written support, withdrawal of this ground for rejection is respectfully requested.

5. Rejection of Claims 17 and 19-22 Under Section 112, First Paragraph, for Alleged Lack of Enablement

Claims 17 and 19-22 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action at page 5. Applicants respectfully traverse the rejection.

In support of this ground for rejection, the examiner states that "while being enabling for a method of assaying the claimed protein with an antibody molecule, [the specification]

does not reasonably provide enablement for the claimed method with a protein binding molecule." The examiner contends that 'a protein binding molecule' includes any molecule that will bind to the protein consisting of the amino acid sequence of accession number Y08612. The specification teaches that protein binding molecules may be natural antibodies or recombinant antibodies such as chimeric proteins that exhibit homology to antibodies." However, the examiner concludes that "one cannot extrapolate the teaching of the specification to the scope of the claims because no protein binding molecules other than antibody constructs are taught."

Applicants disagree with the examiner's interpretation of the specification, but for the purposes of expediting prosecution have amended the claims to recite "antibody." Applicants have also added claim 29 which recites that the "antibody" of claim 17 "is a natural antibody, a recombinant antibody or a chimeric protein." This claim is supported by the present specification and by the examiner's statements of the present Office Action.

Accordingly, applicants respectfully request that the rejection be withdrawn.

6. Rejection of Claims 18 and 24 Under Section 112, First Paragraph, for Alleged Lack of Enablement

Claims 18 and 24 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action at page 6. Applicants respectfully traverse the rejection.

The examiner states that the step of "annealing a nucleic acid binding molecule to a nucleic acid transcript encoding said protein" "includes a whole universe of nucleic acid transcripts since the degeneracy of the code is notoriously well known in the art."

Applicants respectfully disagree with the examiner. Applicants state explicitly, at page 6 lines 7-11, that "[T]he determination of overexpression of the protein Nup88 using nucleic acid binding molecules binding to the transcript of Nup88 can be performed using methods well known in the art like polymerase chain reaction (PCR), including RT-PCR, hybridization techniques, including northern [sic] blot hybridization and other techniques suitable for the measurement of mRNA transcripts."

The skilled artisan, in attempting to perform the methodological step recited in claim 18, would not resort to "a whole universe of nucleic acids" from which to pick a polynucleotide to anneal to the Nup88 transcript as required by claim 18. Instead, the skilled

artisan would, in order to detect the presence of a Nup88 nucleic acid transcript, select a nucleic acid sequence that is capable of specifically annealing to the Nup88 transcript, *i.e.*, they would select some nucleic acid molecule that is *complementary* to a part of the Nup88 transcript. The cited techniques, *e.g.*, PCR, Northern blotting, and hybridization methods, in keeping within the context of the present invention, require the use of a nucleic acid sequence that specifically detects the Nup88 transcript. Accordingly, given Applicants disclosure, the skilled artisan would obtain or design a nucleic acid that would anneal, in complementary fashion, to a part of the DNA sequence described for accession number Y08612.

Applicants are not required to explicitly detail every conceivable nuance of their claimed invention that is already known or apparent to the skilled artisan. The skilled artisan knows that, for a nucleic acid to be useful for performing the claimed invention, it must be capable of specifically detecting a Nup88 transcript from a cell sample. A purpose of the claimed invention is to detect Nup88 protein and/or its nucleic acid transcript so as to determine whether it is overexpressed. The present invention does not entail the detection of a "whole universe" of proteins or transcripts. Consequently, the claimed invention does not entail the use of "a whole universe" of transcripts to anneal to a Nup88 nucleic acid. The claimed invention entails the use of a nucleic acid molecule that can specifically detect Nup88 transcripts. Applicants have amended claims 18 and 24 to recite the word "specifically."

For at least these reasons, the examiner's rejection should be withdrawn.

7. Rejection of Claims 18 and 24 under Section 112, First Paragraph, for Alleged Lack of Enablement

Claims 18 and 24 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action at page 7. Applicants respectfully traverse the rejection.

The examiner believes that even if applicants overcame the rejection given above under section III.A.6., claims 18 and 24 are still unpatentable because "it is well known in the art that expression levels of proteins are neither necessarily dictated by, nor predictable from, the expression of nucleic acid molecules." The examiner then cites a number of publications to support this allegation.

The examiner's rejection is overcome by established scientific evidence that it is

well-known how to correlate nucleic acid transcript levels to that of the encoded protein. For example, Orntoft *et al.*, *Mol. Cell. Proteomics, 1*:37-45 (2002), showed that there was good correlation between gene copy numbers, transcripts, and protein levels in non-invasive and invasive human transitional cell carcinomas. Negro *et al.*, *Mol. Brain Res., 48*:30-36 (1997), showed that there existed a correlation between the mRNA and protein levels of TIMP-2 and MMP-2 in response to treatment of samples with ciliary neurotrophic factor. Granot *et al.*, *Mol. Reprod. Dev., 47*:231-239 (1997), showed a direct correlation between Cx43 protein levels and the level of expression of the encoding gene. Dozin *et al.*, *Biochemistry, 24*:5581-5586 (1985), illustrated that the levels of rat liver malic enzyme and its encoding gene can both be artificially increased. And finally, Moen *et al.*, *J. Biol. Chem., 254*:3526 (1979), showed that the increase in procollagen synthesis is directly proportional to an increase in procollagen mRNA levels.

It is clear then, that the examiner's contention that it is impossible to correlate levels of nucleic acid in a cell with overexpression of the encoded protein is unfounded. For at least this reason, Applicants respectfully request withdrawal of this ground for rejection.

8. Rejection of Claims 21 and 22 Under Section 112, First Paragraph, for Alleged Lack of Enablement

Claims 21 and 22 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action at page 8. Applicants respectfully traverse the rejection.

The examiner alleges that the specification "does not reasonably provide enablement for a method using a chimeric protein wherein said chimeric protein comprises at least one CDR region of the monoclonal antibody" of DSM ACC 2457. According to the examiner, "[t]he specification fails to ... teach how to make the claimed chimeric protein so that it will function as claimed."

Applicants respectfully disagree. The skilled artisan is well aware of the established methods in this field of art that describe how to create a chimeric protein. It is well within the purview of the skilled artisan to compare chimeric proteins with others to determine the extent to which the new chimeras function as desired; *i.e.*, the chimeric antibody can be compared with the monoclonal antibody using standard immunological assays to determine their suitability.

There are a variety of examples that chimeric antibodies bearing only small parts of a complete antibody are sometimes superior over their monoclonal counterparts, since they are easier to manipulate and are more capable of penetrating cells due to their smaller size. Furthermore, chimeric antibodies are widely used for treating various cancer and autoimmune diseases. Accordingly, the skilled artisan is well aware of how to create and use "chimeric proteins" in accordance with the claimed invention.

Thus, claims 21 and 22 are enabled and withdrawal of this ground for rejection is respectfully requested.

9. Rejection of Claims 27 and 28 Under Section 112, First Paragraph

Claims 27 and 28 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action at page 12. Applicants respectfully traverse the rejection.

The examiner contends that claims 27 and 28 are not enabled because the specification "does not reasonably provide enablement for a part of the sequence/antigenic part for use as a control sample."

Applicants have cancelled claims 27 and 28, without prejudice or disclaimer thereof. This ground for rejection is moot.

B. Rejection of Claims 13-28 Under Section 112, Second Paragraph

Claims 13-28 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. Office Action at page 15. Applicants respectfully traverse the rejection.

The examiner stated that claims 13-28 are indefinite because they "recite a GeneBank accession number ["Y08612"] and the sequences corresponding to GeneBank accession numbers can be modified, changed and/or updated. Thus, the sequence may vary or change over time."

Applicants have inserted into the specification and into the requisite claims the specific sequence of the Nup88 protein described in GeneBank accession number Y08612.

Continuing, the examiner states that claims 21 and 22 are indefinite because of the recitation of the word "chimeric." That term "chimeric" is, in fact, a well-established term of

art, with which the skilled artisan is familiar. Chimeric antibodies are already approved by the U.S. Food and Drug Administration for use in therapy, for instance. Accordingly, the recitation of the term "chimeric" in claims 13-28 does not render the claims indefinite.

Claims 23, 25, and 26 have been amended and, therefore, the issue with respect to incorrect antecedent basis is moot.

Withdrawal of this ground for rejection is respectfully requested.

C. Rejection of Claim 24 Under 35 U.S.C. § 102(b)

Claim 24 was rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Boehringer Mannheim Biochemicals Catalog, p. 93 (1994). Office Action at page 16. Applicants respectfully traverse the rejection.

The examiner alleged that claim 24 is anticipated by the Boehringer Mannheim catalog, which teaches a kit comprising random primers that encompass all possible 6-nucleotide sequences, a subset of which will anneal to every nucleic acid transcript.

Applicants have amended claim 24 to recite that the nucleic acid molecule anneals specifically to the Nup88 transcript. "Specifically" is understood by the skilled artisan to mean that the nucleic acid molecule is complementary to and anneals to the Nup88 transcript alone and to no other transcript present in the cell. A "random primer" as taught by the Boehringer Mannheim catalog will not bind specifically to the Nup88 transcript, but will also bind to others present in the cell.

Accordingly, claim 24 is not anticipated by the cited reference and, therefore, withdrawal of this ground for rejection is respectfully requested.

IV. Conclusion

The claimed invention is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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MARKED-UP VERSION OF THE CLAIMS

13. (Once amended) A method for identifying a cancer cell comprising:

(a) providing a tissue biopsy sample; and

(b) determining the level of expression in the sample of the protein consisting of the amino acid sequence:

MAAAEGPVGDGELWQTWLPNHVVFLRLREGLKNQSPTEAEKPASSSLPSSPPPQLLTRNVVFGLGGEL
FLWDGEDSSFLVVRLRGPSGGGEEPALSQYQRLLCINPPLFEIYQVLLSPTQHHVALIGIKGLMVLEL
PKRWGKNSEFEGGKSTVNCSTTPVAERFFTSSTSLTLKHAAWYPSEILDPHVVLLTSDNVIRIYSLRE
PQTPTNVIILSEAEEESLVLNKGRAYTASLGETAVAFDFGPLDAVPKTLFGQNGKDEVVAYPLYILYE
NGETFLTYISLLHSPGNIWKAVGSIAHASAAEDNYGYDACAVLCLPCVPNILVIATESGMLYHCVVLE
GEEEDDHTSEKSWDSRIDLIPSLYVFECVELELALKLASGEDDPFDSDFSCPVKLHRDPKCPSRYHCT
HEAGVHSVGLTWIHKLHKFLGSDEEDKDSLQELSTEQKCFVEHILCTRPLPCRQPAPIRGFWIVPDIL
GPTMICITSTYECLIWPLLSTVHPASPPLLCTREDVEVAESSLRVLAETPDSFEKHIRSILQRSVANP
AFLKASEKDIAPPPEECLQLLSRATQVFREQYILKQDLAKEEIQRRVKLLCDQKKKQLEDLSYCREER
KSLREMAERLADKYEEAKEKQEDIMNRMKKLLHSFHSELPVLSDSERDMKKELQLIPDQLRHLGNAIK
QVTMKKDYQQQKMEKVLSLPKPTIILSAYQRKCIQSILKEEGEHIREMVKQINDIRNHVNF

[of Accession number Y08612 in said sample], wherein a sample comprising [the protein bearing Accession number Y08612] said protein at a level of expression that is [between 1.5 to 5 times] greater than non-cancer cells [normal] indicates that said sample comprises [, is indicative of] a cancer cell.

17. (Once amended) The method of claim 13, wherein the step of determining the level of expression of said [the] protein consisting of said [the] amino acid sequence [of accession number Y08612,] comprises binding an antibody [a protein-binding molecule] to said protein.

18. (Once amended) The method of claim 13, wherein the step of determining the level of expression of said [the] protein consisting of said [the] amino acid sequence [of Accession number Y08612] comprises annealing of a nucleic acid binding molecule specifically to a nucleic acid transcript encoding said protein.

19. (Once amended) The method of claim 17, wherein said antibody [protein binding molecule] is a monoclonal antibody directed against said protein.

20. (New) The method of claim 19, wherein said monoclonal antibody is the monoclonal antibody bearing the biological deposit accession number DSM ACC 2457.

21. (Once amended) The method of claim 17, wherein said antibody [protein binding molecule] is a chimeric protein [of accession number Y08612].

23. (Once amended) A diagnostic kit [for carrying out the method of claim 13,] comprising [materials and reagents for determining the amount of] a protein binding molecule [in a tissue biopsy sample], wherein the protein binding molecule binds to the protein consisting of the amino acid sequence:

MAAAEGPVGDGELWQTWLPNHVVFLRLREGLKNQSPTEAEKPASSSLPSSPPPQLLTRNVVFGLGGELF
LWDGEDSSFLVVRLRGPSGGGEEPALSQYQRLLCINPPLFEIYQVLLSPTQHHVALIGIKGLMVLELPK
RWGKNSEFEGGKSTVNCSTTPVAERFFTSSTSLTLKHAAWYPSEILDPHVVLLTSDNVIRIYSLREPQT
PTNVIILSEAEEESLVLNKGRAYTASLGETAVAFDFGPLDAVPKTLFGQNGKDEVVAYPLYILYENGET
FLTYISLLHSPGNIWKAVGSIAHASAAEDNYGYDACAVLCLPCVPNILVIATESGMLYHCVVLEGEEED
DHTSEKSWDSRIDLIPSLYVFECVELELALKLASGEDDPFDSDFSCPVKLHRDPKCPSRYHCTHEAGVH
SVGLTWIHKLHKFLGSDEEDKDSLQELSTEQKCFVEHILCTRPLPCRQPAPIRGFWIVPDILGPTMICI
TSTYECLIWPLLSTVHPASPPLLCTREDVEVAESSLRVLAETPDSFEKHIRSILQRSVANPAFLKASEK
DIAPPPEECLQLLSRATQVFREQYILKQDLAKEEIQRRVKLLCDQKKKQLEDLSYCREERKSLREMAER
LADKYEEAKEKQEDIMNRMKKLLHSFHSELPVLSDSERDMKKELQLIPDQLRHLGNAIKQVTMKKDYQQ
QKMEKVLSLPKPTIILSAYQRKCIQSILKEEGEHIREMVKQINDIRNHVNF

[of Accession number Y08612].

24. (Once amended) A diagnostic kit [for carrying out the method of claim 13,] comprising [materials and reagents for performing and determining the amount of] a nucleic acid [in a tissue biopsy sample], wherein the nucleic acid anneals specifically to a nucleic acid transcript that encodes the protein consisting of the amino acid sequence:

MAAAEGPVGDGELWQTWLPNHVVFLRLREGLKNQSPTEAEKPASSSLPSSPPPQLLTRNVVFGLGGELF
LWDGEDSSFLVVRLRGPSGGGEEPALSQYQRLLCINPPLFEIYQVLLSPTQHHVALIGIKGLMVLELPK
RWGKNSEFEGGKSTVNCSTTPVAERFFTSSTSLTLKHAAWYPSEILDPHVVLLTSDNVIRIYSLREPQT
PTNVIILSEAEEESLVLNKGRAYTASLGETAVAFDFGPLDAVPKTLFGQNGKDEVVAYPLYILYENGET
FLTYISLLHSPGNIWKAVGSIAHASAAEDNYGYDACAVLCLPCVPNILVIATESGMLYHCVVLEGEEED
DHTSEKSWDSRIDLIPSLYVFECVELELALKLASGEDDPFDSDFSCPVKLHRDPKCPSRYHCTHEAGVH
SVGLTWIHKLHKFLGSDEEDKDSLQELSTEQKCFVEHILCTRPLPCRQPAPIRGFWIVPDILGPTMICI

TSTYECLIWPLLSTVHPASPPLLCTREDVEVAESSLRVLAETPDSFEKHIRSILQRSVANPAFLKASEK
DIAPPPEECLQLLSRATQVFREQYILKQDLAKEEIQRRVKLLCDQKKKQLEDLSYCREERKSLREMAER
LADKYEEAKEKQEDIMNRMKKLLHSFHSELPVLSDSERDMKKELQLIPDQLRHLGNAIKQVTMKKDYQQ
QKMEKVLSLPKPTIILSAYQRKCIQSILKEEGEHIREMVKQINDIRNHVNF

[of Accession number Y08612].

25. (Once amended) The kit of claim 22 [21] further comprising in whole or in part, the protein consisting of said amino acid sequence [of Accession number Y08612], for use as a control sample.

26. (Once amended) The kit of claim 24 [22] further comprising in whole or in part, the protein consisting of said [the] amino acid sequence [of Accession number Y08612], for use as a control sample.